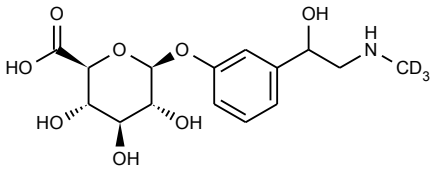
BDG SYNTHESIS

Certificate of Analysis

BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
3 October 2011

Name:	**(*R*/*S*)-Phenylephrine-d_3 Glucuronide**
CAS Number:	none
Structure:	
Molecular Weight:	$C_{15}H_{18}D_3NO_8$ = 346.35
Lot Number:	BDG 13269.4
Appearance:	White, amorphous solid
Corrected Purity:	100.0 % (HPLC) - 4.4 % (water) = 95.6 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	3 October 2016

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
Light:	protect from strong sunlight.
Caution:	only experienced laboratory personnel should handle the material.

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: signals at the site of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.
Residual Solvents: no residual solvents are observed.
Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: signals at the site of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 347.1533. $C_{15}H_{19}D_3NO_8$ $[M+H]^+$ requires *m/z* 347.1534. The deviation of 0.3 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for d_0 material was seen (detection limit about 0.5 %).

HPLC

Two sharp, symmetrical peaks are observed (100 %). The first-eluting peak is identified as (*R*)-Phenylephrine-d_3 Glucuronide by spiking experiments. The non-integrated peaks are present in the solvent blank. Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis

	Found:	C 49.45, H 5.41, D 1.62, N 3.76 %
$C_{15}H_{18}D_3NO_8 \cdot 0.9H_2O$	Requires:	C 49.69, H 5.50, D 1.67, N 3.86 %
$C_{15}H_{18}D_3NO_8$	Requires:	C 52.02, H 5.24, D 1.74, N 4.04 %

The elemental analyses fall substantially outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given.

Karl-Fischer Analysis

	Found:	H_2O 4.4 %
$C_{15}H_{18}D_3NO_8 \cdot 0.9H_2O$	Requires:	H_2O 4.5 %

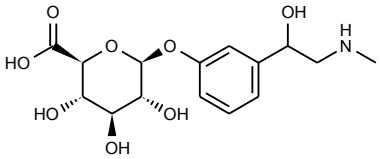
Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

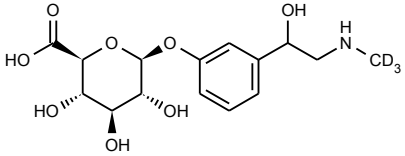
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.

BDG SYNTHESIS

Proton NMR Spectrum of (*R*/*S*)-Phenylephrine Glucuronide (top) and (*R*/*S*)-Phenylephrine-d_3 Glucuronide (bottom) in D_2O





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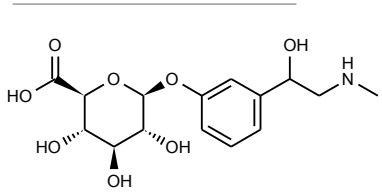
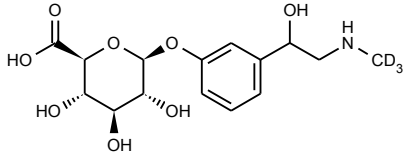
BDG SYNTHESIS

Carbon-13 NMR Spectrum of (*R*/*S*)-Phenylephrine Glucuronide (top) and (*R*/*S*)-Phenylephrine-d_3 Glucuronide (bottom) in D_2O





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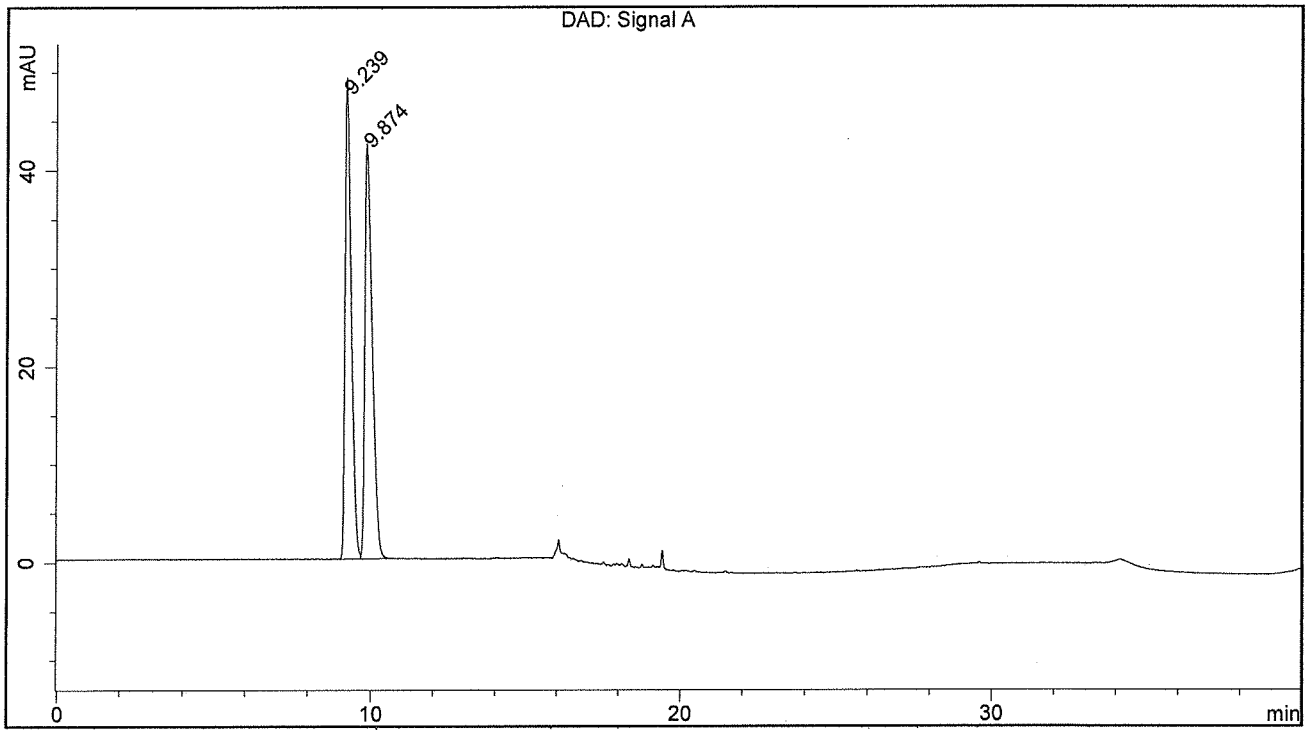
BDG - Analysis of Phenylephrine-d3 Glucuronide

Column : YMC-Pack ODS-AQ 5 um 250 x 4.6 mm I.D.
Guard : Phenomenex Security Guard AQ C18 4 x 3 mm
Mobile Phase A : Water + 0.01% Trifluoroacetic Acid
Mobile Phase B : Acetonitrile + 0.01% Trifluoroacetic Acid
Gradient (A:B) : T0 = 100:0, T10 = 99:1, T25 = 10:90, T30 = 10:90, T35 = 100:0 , T40 = 100:0
Flow Rate : 1.0 mL/min
Sample Solvent : Water
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV 268 nm,

Sample Name	BDG 13269.4	Instrument	AnalyticalLC01
Acquisition	03/10/2011, 22:57:44	Method (rev.)	LC10224g (6)
Sequence	BDG_03Oct2011e - Reprocessed	Vial Position	42
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	9.24 min	48.9940	670.1731	0.2056 min	49.403 %
2	9.87 min	42.2956	686.3734	0.2393 min	50.597 %